

REMARKS/ARGUMENT

Claims 1, 4, 15, 17, 22-23, 26, 36-37, 49-51, and 53-56 stand rejected under 35 U.S.C. 103(a) as being unpatentable over the Obara et al. article in Volume 126 of the *International Journal of Pharmaceutics* ("Obara") in view of Akiyama et al. U.S. Patent No. 5,576,025 ("Akiyama"). Obara discloses methods for forming free films of HPMCAS from aqueous dispersions thereof by spraying such dispersions onto Teflon sheets attached to a heated rotating drum. Obara, Section 2.4. Akiyama discloses coated matrix particles wherein the matrix is solid at ambient temperature, and comprises an active ingredient such as a drug, a viscogenic agent (such as an acrylic acid polymer) that is capable of developing viscosity on contact with water and a polyglycerol fatty acid ester or a lipid. See Akiyama Abstract.

Akiyama's exemplary viscogenic agents are polymers containing carboxyl groups or salts thereof, cellulose ethers, PEGs of MW $\geq 200,000$ and naturally occurring mucous substances. Akiyama at column 1, lines 14-23. Exemplary polymers containing carboxyl groups or salts thereof are acrylic acid polymers. *Ibid* at column 1, lines 36-37. Exemplary cellulose ethers are CMC sodium, HPMC, methylcellulose and crystalline cellulose-CMC sodium. *Ibid* at column 1, lines 58-66. Exemplary naturally occurring mucous substances are listed in the first paragraph of column 4. Therefore HPMCAS is not a viscogenic agent according to Akiyama. When the Akiyama matrix is in the form of particles, they may be coated with at least the viscogenic agent, but the coating may also contain at least one of a fatty acid ester, a lipid, an enteric polymer and a water-insoluble polymer such as HPMCAS. Akiyama at column 11, lines 46-51 and 58-61. Thus, at best, when the Akiyama matrix particles include HPMCAS in the coating, they must also be coated with the viscogenic agent.

The §103 rejection is respectfully traversed for the following reasons.

First, assuming for purposes of argument that Akiyama discloses spray-dried coated matrix particles containing a poorly water soluble drug, the particles consist of at least one more essential ingredient beyond the drug and HPMCAS, namely, the viscogenic agent. In this connection the Examiner's attention is directed to the wording of applicants' independent claims 1 and 15, namely, that the dispersion "consists essentially of" low solubility drug and HPMCAS. It is well-settled that the transitional phrase "consisting essentially of" limits the scope of the claim to the specified materials and those that do not materially affect the basic and novel characteristics of the claimed invention. *In re Herz*, 190 USPQ 461, 463 (CCPA 1976). Here, since Akiyama's viscogenic agent is a key ingredient in adhering the composition to gastrointestinal mucosa so as to prolong the duration of a drug's activity (column 2, lines 27-33), it may not be characterized as a material that does not affect the basic characteristic of the invention claimed in applicants' claims 1 and 15. Similarly, Obara's aqueous dispersions of HPMCAS all contained plasticizers (Obara, Section 3.1) and since the plasticizers contributed materially to the formation of films (*Ibid*), plasticizers may not be characterized as not affecting the basic characteristic of the claimed invention.

Second, there is no motivation to combination Obara and Akiyama since there is no reasonable expectation that a spray-dried dispersion would result from the combination. *In re Reinhart*, 189 USPQ 143 (CCPA 1976) (evidence showing no reasonable expectation of success supports a conclusion of nonobviousness). Independent claims 1 and 15 of the instant invention are directed to a spray dried solid dispersion consisting essentially of a sparingly water soluble drug and HPMCAS. Conceding for purposes of argument that some of the drugs in Akiyama have poor water solubility, the HPMCAS dispersion of Obara is aqueous; in other words, the Obara solvent is water or at least water-based. One of ordinary skill would have no reasonable

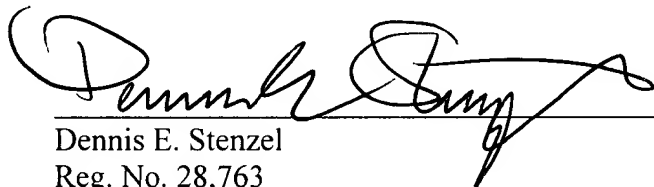
expectation that a poorly water soluble drug combined with a water-based dispersion could form a solution suitable for spray drying since the drug would not be expected to dissolve in the aqueous dispersion.

Finally, claims 1 and 15 also require the solid dispersion to have a drug to polymer weight ratio of between 1:0.4 and 1:20. Neither Obara nor Akiyama disclose such a drug to polymer ratio.

All of the remaining claims of the application depend from claim 1 or 15 or both, and so contain the same limitations as those claims. Accordingly they are not rendered obvious by the combination of Obara and Akiyama for the same reasons given above.

Early and favorable reconsideration is respectfully requested.

Respectfully submitted,

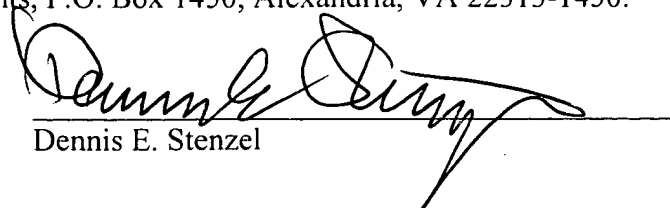


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